Negative Symptoms in Depressed and Schizophrenic Patients: How Do They Differ?

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Background: The present study evaluated differences in negative symptoms between schizophrenic and depressive patients and investigated whether a consideration of the nature of negative symptoms (enduring vs. nonenduring) can help to improve their specificity for schizophrenia.

Method: Patients enrolled in the study were consecutively hospitalized with an acute exacerbation of schizophrenia (N = 33) or major depressive disorder (N = 43) (DSM-IV). Negative and depressive symptoms were assessed with the Scale for the Assessment of Negative Symptoms (SANS) and the Montgomery-Asberg Depression Rating Scale, respectively. Duration of negative symptoms was assessed through a semistructured interview with the patients and their closest relatives. On the basis of the assessed duration of symptoms, negative symptoms were categorized as enduring or nonenduring.

Results: Analyses revealed high SANS ratings for both diagnostic groups. Negative symptoms in depressive patients ($p = .01$), but not in schizophrenic patients, were significantly associated with the presence or the emergence of depressive symptoms. The prevalence of enduring negative symptoms was significantly higher in schizophrenic patients than in depressive patients ($p < .01$). A consideration of enduring negative symptoms significantly increased the discriminative power of negative symptoms for schizophrenia ($p = .02$).

Conclusion: The present findings suggest that negative symptoms in most depressive patients are just an epiphenomenon of depressive symptoms and can be distinguished from schizophrenic negative symptoms.

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Negative symptoms are believed to belong to a core syndrome in schizophrenia. Major international diagnostic criteria (DSM-IV and ICD-10) for schizophrenia include negative symptoms. Nevertheless, negative symptoms have also been described in a variety of other psychiatric disorders, in particular depressive disorders (e.g., references 1–3). These facts represent a serious clinical problem, since the detection of negative symptoms in a patient has diagnostic, prognostic, and therapeutic relevance. To resolve this problem, it should be clarified whether the previously reported high prevalence of negative symptoms in non-schizophrenic patients merely reflects a methodological problem that can be improved, or whether negative symptoms really are present in non-schizophrenic disorders. The present study therefore aimed to evaluate the following hypotheses:

1. The cross-sectional assessment of the severity of negative symptoms reveals comparable results for depressive and schizophrenic patients.
2. Negative symptoms in patients with major depressive disorder, but not in those with schizophrenia, strongly depend on the presence of depressive symptoms.
3. Negative symptoms in patients with major depressive disorder differ in their course and duration and are less often enduring than negative symptoms in schizophrenia.
4. The specificity of enduring negative symptoms for schizophrenia is higher than that of negative symptoms that are cross-sectionally assessed.

METHOD

Patients were enrolled in the present study who were consecutively hospitalized with an acute exacerbation of a schizophrenic or major depressive disorder. Clinical diagnoses of these patients were made during the index hospitalization according to DSM-IV by the means of a consensus among experienced psychiatrists, including at least one person with a professorial degree. All enrolled patients were assessed by experienced psychiatrists during the week after hospitalization using the Scale for the Assessment of Negative Symptoms (SANS)[4] and the

Montgomery-Asberg Depression Rating Scale (MADRS).[5] Thereafter, patients and their closest relatives were separately interviewed by the same psychiatrist and were asked to answer several questions as to how long the negative symptoms, rated as clearly present in the SANS assessment (a score of 2 or more), had been continually present during the 12 months prior to the index hospitalization. Patients and relatives were asked to choose 1 of 5 possible answers: (1) for at least 12 months, (2) for at least 6 months, (3) for at least 3 months, (4) for at least 1 month, (5) the symptom was never present for longer than a few days. To make it easier for patients and relatives to understand the respective symptoms, interviewers gave a standardized explanation of each SANS symptom in everyday language. Every patient and relative could identify the symptoms well and completed the additional interview concerning the duration of negative symptoms. In total, 33 schizophrenic patients (22 men, 11 women; mean age = 32.15 ± 9.12 years) and 43 patients with major depressive disorder (19 men, 24 women; mean age = 47.88 ± 10.59 years) took part in the study. Prior to enrollment, subjects gave their informed consent to participate in the study, which had been approved by the local ethics committee. For analyses, the total MADRS and SANS summary scores, as well as the summary score of the global ratings for affective flattening, alogia, avolition-apathy, asociality-anhedonia, and attention deficits, were calculated.

To evaluate differences in the duration of symptoms, the percentage of patients who reported that 1 or more of the global SANS symptoms were present for at least 12, 6, 3, or 1 month(s) prior to the index hospitalization was calculated. The same calculation was performed for the corresponding estimations by relatives. Multivariate analysis of covariance (MANCOVA), controlling for age and gender, was used to assess the effect of diagnosis on the SANS and MADRS ratings. Group differences for categorical variables were estimated by chi-square statistics. Group differences for continuous variables were estimated by 2-tailed t tests. The Spearman rho was used to calculate the correlation between MADRS and SANS scores in schizophrenic and depressive patients separately.

To analyze whether a consideration of enduring negative symptoms improves the power to discriminate between schizophrenic and depressive patients, a hierarchical logistic regression analysis, with diagnostic groups being used as dependent variables, was performed. The total SANS summary score and the duration of negative symptoms, categorized as enduring (duration of symptoms ≥ 12 months) or nonenduring (duration of symptoms < 12 months), were sequentially entered into the analysis. The cutoff point of 12 months for categorizing negative symptoms as enduring or nonenduring is generally used in this field of research.[6] The duration of negative symptoms, as evaluated by patients themselves and relatives, was separately entered after the total SANS summary score. Based on a computed classification table, some discriminative values (sensitivity, specificity, and percentage of correct classifications) were calculated for each step of the analysis. p Values of < .05 (2-tailed) were considered as statistically significant. SPSS 10 (SPSS, Inc., Chicago, Ill.) was used for all statistical analyses.

RESULTS

Comparison of the Severity of Negative Symptoms in Depressive and Schizophrenic Patients

Cross-sectional assessment of negative symptoms revealed a mean ± SD SANS summary score of 55.5 ± 24.4 for schizophrenic patients and 45.7 ± 21.4 for depressive patients. The mean SANS summary score of the global symptoms was 12.9 ± 5.1 for schizophrenic patients and 10.5 ± 4.7 for depressive patients. MANCOVA, controlling for gender and age, indicated nonsignificant differences between schizophrenic and depressive patients (Wilks lambda = 0.92; F = 3.07, df = 2,71; p = .053).

Association Between Negative and Depressive Symptoms in Depressive and Schizophrenic Patients

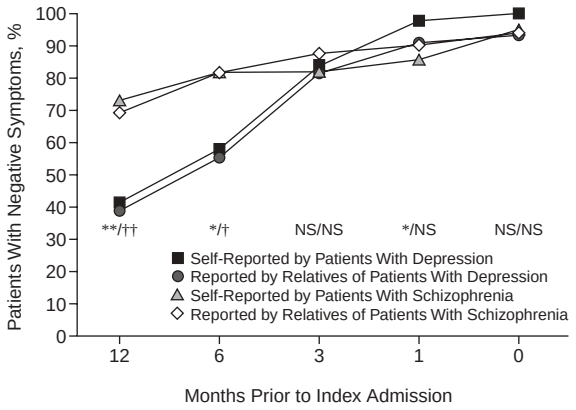
Summary score of the MADRS was 18.3 ± 8.8 for schizophrenic patients and 32.7 ± 8.5 for depressive patients. The difference between both groups, controlling for gender and age, was highly significant (F = 31.94, df = 1,72; p < .001). Correlation analyses between depressive and negative symptoms, controlled for the effects of age and gender, revealed a significant association between both psychopathologic dimensions in the group of depressive patients (partial correlation coefficient = 0.40; p = .01), but not in the group of schizophrenic patients (partial correlation coefficient = 0.15; p = .41).

Comparison of the Course and Nature of Negative Symptoms in Depressive and Schizophrenic Patients

The course of negative symptoms prior to the index hospitalization, as assessed through an interview with the patients and their relatives, is shown in Figure 1. On a descriptive level, the figure demonstrates that in most depressive patients, negative symptoms emerged for the first time during the 3 months prior to the index hospitalization. In contrast, negative symptoms of most schizophrenic patients were already continually present during the 12 months prior to the index admission.

To test our hypothesis that negative symptoms in schizophrenia are more chronic than the probably transient negative symptoms in depressive patients, the nature of the assessed negative symptoms was categorized as "enduring" (duration of at least 1 of the 5 global SANS symptoms was ≥ 12 months) and "nonenduring" (none of the 5 global SANS symptoms had a duration of more than

Figure 1. Percentage of Patients With 1 or More Symptoms (according to global SANS ratings) That Were Continually Present for at Least 12, 6, 3, or 1 Month(s) Prior to Index Hospitalization



*p < .05, **p < .01, significant difference between diagnostic groups in presence of symptoms as reported by patients.
†p < .05, ††p < .01, significant difference between diagnostic groups in presence of symptoms as reported by relatives of patients.
Abbreviations: NS = not statistically significant, SANS = Scale for the Assessment of Negative Symptoms.

12 months). In accordance with the hypothesis, analyses revealed that the percentage of patients with enduring negative symptoms was significantly higher in patients with schizophrenia than in patients with major depression (see Figure 1). This was true for the assessment by patients (73% in schizophrenia vs. 42% in major depression; $\chi^2 = 7.2$, df = 1, p = .007) as well as for the assessment by relatives (70% in schizophrenia vs. 40% in major depression; $\chi^2 = 6.8$, df = 1, p =. 009). Reliability of the assessment of enduring negative symptoms by patients and their relatives was fairly good (intraclass correlation coefficient = 0.69; F = 3.21, df = [75,75], p < .001).

With regard to the observed age and gender differences between the 2 diagnostic groups, we analyzed whether these differences were also present between patients with and those without enduring negative symptoms. Analyses revealed no significant differences, indicating that the presence of enduring negative symptoms was not affected by the age or gender of patients. In detail, we found that enduring negative symptoms were present in 51.4% of female patients and in 58.5% of male patients ($\chi^2 = 0.39$, df = 1, p = .53). The mean age was 41.35 ± 11.65 years in patients with enduring negative symptoms and 40.72 ± 13.83 years in patients without enduring negative symptoms (t = 0.22, df = 74, p = .83).

Specificity of Enduring Negative Symptoms for Schizophrenia

Finally, we analyzed whether consideration of the nature of negative symptoms (enduring or nonenduring) improves their power to discriminate between schizophrenic and depressive patients. For this purpose, a hierarchical logistic regression analysis, with diagnostic groups being used as dependent variables, was performed (Table 1). At Step 1, in which only the SANS summary score was included, the model was not significantly improved from the null model ($\chi^2 = 3.4$, df = 1, p = .07), indicating that the discrimination between schizophrenic and depressive patients was not possible on the basis of the SANS summary score alone. In the second step, the nature of negative symptoms (enduring or nonenduring) was additionally entered into the preceding logistic model. In Step 2a, the categorization of negative symptoms was based on the information given by patients. This step improved the model significantly ($\chi^2 = 5.8$, df = 1, p = .02), indicating that a consideration of the nature of negative symptoms was significantly effective in differentiating between the groups of patients. In Step 2b, the categorization of negative symptoms was based on the information given by relatives. This analysis provided quite similar results to those in Step 2a (see Table 1).

With regard to the differences in age and gender distribution between the 2 diagnostic groups, we performed a further hierarchical logistic regression analysis, which considered the effects of age and gender on the observed model improvements, presented above. In the first step of these analyses, the logistic regression model was adjusted for age and gender. After that, improvement of the adjusted model by the SANS and enduring negative symptoms ratings was determined in the same way as before. The findings of these analyses were quite similar to the findings of the first analyses, indicating that the observed model improvements by the assessment of enduring negative symptoms are not substantially confounded by age and gender differences between the 2 groups of patients (model improvement by the SANS rating: $\chi^2 = 2.9$, df = 1, p = .85; model improvement by enduring negative symptoms [patients]: $\chi^2 = 8.0$, df = 1, p =. 005; model improvement by enduring negative symptoms [relatives]: $\chi^2 = 16.4$, df = 1, p < .001).

DISCUSSION

As reported in previous studies (e.g., references 1 and 2), the present study found that schizophrenic and depressive patients showed similarly high scores in SANS ratings, which did not differ significantly between both groups. This finding indicates that cross-sectionally assessed negative symptoms cannot differentiate between depressive and schizophrenic patients. Consequently, the specificity of negative symptoms obtained by a cross-sectional assessment was rather low (see Table 1). A further result of the present study was that negative symptoms in patients with major depressive disorder, but not in patients with schizophrenia, were significantly associated

Table 1. Discriminative Value of Total SANS Ratings and Duration of Negative Symptoms for Schizophrenia[a]

Entered Variables	Odds Ratio	95% Confidence Interval	p Value	Sensitivity,[b] %	Specificity,[c] %	Discriminative Value (correct classification, %)
Step 1: SANS summary score Model improvement: $\chi^2 = 3.4$, df = 1, p = .07	0.98	0.96 to 1.01	.07	52	60	58
Step 2a: Presence of enduring negative symptoms (according to information given by patients) Model improvement: $\chi^2 = 5.8$, df = 1, p = .02	3.31	1.23 to 8.98	.02	65	71	68
Step 2b: Presence of enduring negative symptoms (according to information given by relatives) Model improvement: $\chi^2 = 6.4$, df = 1, p = .01	3.44	1.29 to 9.18	.01	61	67	65

[a]Dependent variable: diagnosis (1 = schizophrenia, 2 = major depressive disorder).
[b]*Sensitivity* indicates the probability of having a diagnosis of schizophrenia when schizophrenia was predicted on the basis of the assessed variable.
[c]*Specificity* indicates the probability of not having a diagnosis of schizophrenia when schizophrenia was not predicted on the basis of the assessed variable.
Abbreviation: SANS = Scale for the Assessment of Negative Symptoms.

with depressive symptoms. The relative independence of negative and depressive symptoms in schizophrenia was also shown in other studies (e.g., Bottlender et al.).[7] The association of both symptom dimensions in depressive patients points to a substantial phenomenological overlapping between negative and depressive symptoms in this group of patients, which may indicate that negative symptoms in depressive patients are just an epiphenomenon of coexisting or emerging depressive symptoms. This interpretation also seems to be supported by our finding that the increase of the percentage of patients with negative symptoms during the short periods prior to the index hospitalization was much greater in depressive than in schizophrenic patients (see Figure 1). Similar to this finding, Blanchard et al.[8] reported that social anhedonia, which is thought to be associated with the negative symptom dimension, was enduring in schizophrenia, but transient and related to the clinical status in depression. A higher percentage of enduring negative symptoms in schizophrenic patients, compared with depressive patients, was also found in the present analyses.

Interestingly, our results demonstrated that a consideration of enduring negative symptoms, compared with the cross-sectional assessment of negative symptoms alone, significantly improves the specificity of negative symptoms for schizophrenia. This improvement, however, was only modest in size. A possible explanation for this limitation is that enduring negative symptoms may not only be restricted to schizophrenia, but may also be present in patients with major depression (about 40%). Comparable observations concerning the presence of enduring negative symptoms in patients with major depressive disorders have been reported by Gerbaldo et al.[9] and Husted et al.[10] It could plausibly be suggested that enduring negative symptoms in depressive patients are probably a reflection of residual depressive symptoms, which were shown by other authors[11,12] to occur for periods of more than 1 year in a substantial number of patients who remitted from their major depressive episodes.

To summarize, the present findings suggest that negative symptoms in most depressive patients are just an epiphenomenon of depressive symptoms and can be distinguished from schizophrenic negative symptoms. The findings also provide evidence that the standardized assessment of the duration of negative symptoms (enduring vs. nonenduring) by patients and their relatives could be helpful to discriminate schizophrenic negative symptoms from those negative symptoms that are most likely to be a mere reflection of a depressive symptomatology. The fact that this discrimination was not possible on the basis of a cross-sectional assessment of negative symptoms alone points to questions concerning the validity of the assessment by the available and widely used assessment instruments for negative symptoms and the need for further methodological improvement in this field of research.[13,14]

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